Biosafety for Viral Gene Therapies

Erich Bozenhardt, PE | Process Manager | IPS – Integrated Project Services LLC | ebozenhardt@ipsdb.com

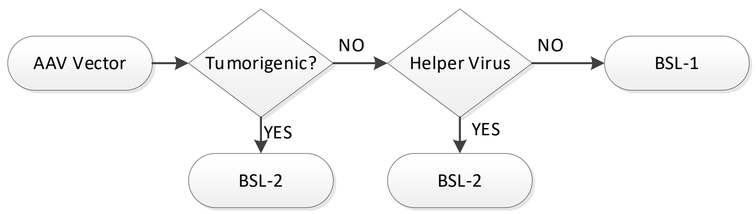
Abstract

With a maturing pipeline of Gene Therapies, companies are developing commercial manufacturing spaces at a rapid rate. The novel processes/organisms are challenging companies to develop a look at their Biosafety operational practices, how those practices and GMP compliance influence the design of facilities. This poster will help build an understanding of how to classify vectors/cell lines, how risk groups translate into facility design, and what GMP practices around containment need to be considered for viral gene therapies.

Identify / Assess

US NIH/CDC Risk Group 1

- Not known to cause disease in healthy humans
- Minimal potential hazard to personnel and the environment
- Most Adeno Associated Virus (AAV)
- E. coli, Saccharomyces cerevisiae, SF9



US NIH/CDC Risk Group 2

- Agents associated with human diseases, but rarely serious
- Preventative or therapeutic interventions are often available
- Moderate potential hazard to humans and environment
- Adenovirus (AV), AAV w/ helper virus, Lentivirus
- All primary human cells, Most human culture cell lines (e.g. HeLa), SV40 or AV modified cell lines (e.g. HEK-293)

Agent classification varies according to national regulation

Operator/Environment

General Practice

- BSL level needs to add one level of separation for each numerical level of the BSL designation
- This protects the operators, the product and the environment
- Each layer must be an envelope of containment

Primary Containment (Equipment)

- Closed Systems
  - Aseptic connectors
  - Tube welding
  - Consider disassembly by tube sealing
- Functionally Closed Systems
  - Closure before charging virus
  - Sanitize post use
- Open Systems
  - Biological Safety Cabinets
  - Sanitize materials and gloves as leaving

Secondary Containment (Facility)

- Hand wash sink at exit
- Self closing doors
- Appropriate Personal Protective Equipment (e.g. masks for airborne agents)
- Approved method of decontaminated waste
  - Autoclave in building
  - Closed drain system w/ inactivation system for larger scale
  - Chemical (verify local expectations)
  - Off-site Inactivation (verify local expectations)
- Movement of contaminated materials in appropriate containers
  - Waste in sealed bag moved on cart with spill containment

Product

GMP Segregation

- Virus / Virus free within train
- Between products in a facility
  - Spatial
  - Air flow
  - Procedural / Personnel

Facility Considerations

- More but smaller air handlers
- Inward air flow to contain (bubble/sink airlocks)
- Air can be recirculated via HEPA
- Fumigation of suite
  - Between products
  - Before the boundary is breached for maintenance
- Maximize the use of unidirectional flow
  - Time segregation for infrequent movements

Conclusion

- Review local regulations.
- Carefully consider the containment boundaries.
- Maximize closed processing.
- Develop robust waste handling practices.
- Segregate and plan for fumigation within the suite boundary.

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